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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/804,760	03/19/2004	Meir S. Sacks	MSS 65055	7688

7590 07/13/2007

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EXAMINER	
VAKILI, ZOHREH	
ART UNIT	**PAPER NUMBER**
1614	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/804,760	SACKS ET AL.	
	Examiner	Art Unit	
	Zohreh Vakili	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 4-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____

DETAILED ACTION

Applicant's Amendment filed March 23, 2007 has been received and entered into the present application. Accordingly, claims 1 and 4 are currently amended. Claims 2-3 are cancelled. Claims 6-10 are newly added. Claims 1, 4-10 are pending and are herein examined on the merits.

Applicant's arguments, filed March 23, 2007, have been fully considered. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Maintained Claim Rejections - 35 USC § 103

The rejection of claims 1, 4-10 under 35 U.S.C. 103(a) over Peeters (WO 94/00132) in view of Howard et al. (GB 2 280 110) has been maintained for the reasons stated in the prior Office Action, November 21, 2006.

Response to Arguments under 35 USC § 103

Applicant's arguments filed March 23, 2007 have been fully considered but they are not persuasive. Applicants argue that obviousness can not be made against the instant claims over Peeters (WO 94/00132) in view of Howard et al. (GB 2 280 110) as such references fail, either alone or in combination to teach that which applicants are

claiming, namely a method for treating Alzheimer disease with uric acid precursor and selected antioxidant. However, upon further consideration, a new ground(s) of rejection is made.

Claim Rejections - 35 USC § 103 (New Grounds of Rejection)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Peeters (WO 94/00132) in view of Howard et al. (GB 2 280 110) and further inview of Ronzio et al.

Peeters discloses the treatment of Alzheimer's disease with guanosine and precursors and/or derivatives thereof, including the elected species xanthosine, as well as guanine, inosine, xanthine, hypoxanthine, 5' inosinic acid, and mono-, di- and triphosphates of guanosine. See claims 1-12, and amended claims 1-12, at pages 14-17 of the English language translation provided herewith. Thus, Peeters discloses pharmaceutical compositions comprising each of those compounds.

Claim 1 recite that the compositions contain a "daily dosage amount" of from 100 to less than 1,000 mg. Properly construed at its broadest, the recitation "daily dosage amount" is merely a recitation of intended use, and the claims encompass any composition which can be administered at the claimed daily rate of administration.

Peeters does not explicitly disclose the amounts of any dosage forms, although Peeters does disclose that oral dosage forms such as tablets and gelcaps are suitable for the disclosed compositions. See page 11 of the translation. Peeters also discloses that the elected species xanthosine should be administered at dosages of from 20 mg/kg/day to 150 mg/kg/day. See translation at page 11, lines 3 and 4. Assuming a 50 kg person, this dosage would result in an administration of compositions comprising 1 to 7.5 grams per day. The artisan of ordinary skill clearly would have recognized that a suitable method of administering 1 gram of xanthosine, or more, per day would have been by administering in 500 mg oral dosage forms. Official notice is taken of the fact that the determination of suitable dosage regimens for the therapeutic methods in Peeters, including the use of 500 mg dosage forms, was clearly well within the purview of the artisan of ordinary skill at the time of applicant's invention. Therefore, the claims

must be considered obvious under § 103(a), absent some demonstration of an unexpected result coming from the claimed use of dosage forms containing less than 1 gram, or no more than 500 mg of xanthosine.

As discussed above, Peeters renders obvious the treatment of Alzheimer's disease using compositions comprising the claimed amounts of guanosine and precursors and/or derivatives thereof, including the elected species xanthosine, as well as guanine, inosine, xanthine, hypoxanthine, 5' inosinic acid, and mono-, di- and triphosphates of guanosine. Peeters differs from the claims in that Peeters does not disclose the inclusion of the elected additional ingredient vitamin C in described compositions.

However, Howard et al. discloses that vitamin C should be included in a regimen of treating Alzheimer's. See claim 5 on page 27, also claim 14 on page 29. Thus, the artisan of ordinary skill, reasonably expecting the vitamin C of Howard et al. to be beneficial in Peeters' method of treating Alzheimer's, clearly would have been motivated to have included Howard's et al. vitamin C in the therapeutic regimen disclosed by Peeters.

Ronzio et al. teach free radicals and oxidative stress, that is the overproduction of reactive oxygen-containing molecules, has been associated with nearly 100 disorders, including certain types of cancer, retinal degeneration, cardiovascular disease, neurodegenerative diseases, ischemia-reperfusion, autoimmune conditions and other conditions associated with chronic inflammation. Whether or not free radicals or reactive oxygen species are a cause or a consequence of the condition, there are

strong indications that antioxidant supplementation can at least ameliorate several of these conditions, (see col. 1, lines 63-67 & col. 2, lines 1-5). Antioxidants to inhibit the oxidation of water soluble nutrients, such as vitamin C, and essential fatty acids, such as linoleic acid, are desirable for improving human nutrition. Antioxidants are also desirable for their use in treating disease and in slowing the aging process. Natural antioxidants which can be derived from an inexpensive food source are especially sought after (see col. 2, lines 32-38). The antioxidant composition extract contains phenolics that are predominantly in the form of polyphenols, including flavonoids and phenolic acids (see col. 5, lines 35-36). The extract is highly effective in stabilizing linoleic acid and in maintaining ascorbic acid (vitamin C) in a reduced state (see col. 6, lines 31-33). The reduction of superoxide was obtained by hypoxanthine-xanthine oxidase and NBT--The reaction mixture contained hypoxanthine: 0.5 mM and with xanthine-xanthine oxidase and NBT--The reaction mixture contained xanthine: 0.5 mM (see col. 10, lines 15-20). Inhibition of oxidation of vitamin C is done by incorporating LHME. Thus, LHME protects vitamin C in solution from oxidation, providing a greater amount of vitamin C available to work as an antioxidant and polyphenols from the LHME can work synergistically with the vitamin C (see col. 11, lines 8-11).

The intended rate of administration does not, and cannot, change the product itself. Thus, despite the recitation in claim 1 regarding a "daily dosage"; all that the claim requires is that the composition comprises the claim-designated amounts of the therapeutic ingredient. One of ordinary skill preparing orally administrable compositions according to Peeters disclosure clearly would have been motivated to have prepared

those compositions in dosage forms containing amounts of the ingredients which would have been suitable for oral administration. Such dosage forms clearly encompass the amounts of hypoxanthine, xanthine and/or inosine recited in the pending claims. Because the intended dosage regimen does not change the product itself, and because Peeters suggests preparing dosage forms containing the claimed amount of uric acid precursors.

Clearly, the skilled artisan is provided with ample instruction and motivation to use the teachings of Ronzio et al. along with the teachings of Peeters. Ronzio et al. teach a mixture rich in polyphenols and vitamin C beneficial in treating neurodegenerative diseases, for example Alzheimer and also in slowing the aging process. Thus, the artisan of ordinary skill, reasonably expecting the vitamin C and polyphenol of Ronzio et al. to be beneficial in Peeters' method of treating Alzheimer's. The skilled artisan is clearly motivated to have included Howard's et al. Vitamin C, Ronzio's et al. polyphenols and Vitamin C in the therapeutic regimen disclosed by Peeters

Note that it is well known that it is *prima facie* obvious to combine two or more ingredients each of which is taught by the prior art to be useful for the same purpose in order to form a third composition which is useful for the same purpose. The idea for combining them flows logically from their having been used individually in the prior art. *In re Pinten*, 459 F.2d 1053, 173 USPQ 801 (CCPA 1972); *In re Susi*, 58 CCPA 1074, 1079-80; 440 F.2d 442, 445; 169 USPQ 423, 426 (1971); *In re Crockett*, 47 CCPA 1018, 1020-21; 279 F.2d 274, 276-277; 126 USPQ 186, 188 (1960).

Thus the claimed invention was within the ordinary skill in the art to make and use at the time the claimed invention was made and as a whole, prima facie obvious.

Applicant's amendment necessitated the new ground(s) of rejection. Applicant amended claim 1 and newly added claims 6-10. The addition of Ronzio et al. is used to modify the rejection because Ronzio et al. teach the use of polyphenols and Vitamin C along with hypoxanthine and xanthine beneficial for treating neurodegenerative diseases.

Applicant argues that Peeters' reference does not raise a prima facie case of obviousness of the presently claimed invention, reading the relatively high levels of uric acid precursors required to be administered by Peeters would not be led to treat an Alzheimer's patient less than 1000 mg of hypoxanthine or xanthine. Examiner does not agree that the determination of a dosage of the active ingredient is not within the level of one having ordinary skill in the art. However, not only the dosage amount is being taught by Peeters, Ronzio et al also teaches the incorporation of 0.50 mM of hypoxantine or 0.5 mM of xanthine. The determination of a dosage of the active ingredient are well within the level of one having ordinary skill in the art, and the artisan would be motivated to determine optimum amounts to get the maximum effect of the drug while minimizing adverse or unwanted side effects or even undesirable stability issues. Therefore with teachings of Peeters and Ronzio et al. the optimum of the dosage have been obvious to the skilled artisan.

Applicant's remarks have been fully and carefully considered in their entirety, but fail to be persuasive.

For these reasons, and those already made of record in the previous Office Action dated November 21, 2007 of which such reasons are incorporated herein by reference, rejection of claims 1-10 remain proper.

Conclusion

No claims of the present application are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office Action. Accordingly, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136 (a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zohreh Vakili whose telephone number is 571-272-3099. The examiner can normally be reached on 9am to 6:00pm Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Examiner
Zohreh Vakili
Art Unit 1614

July 2, 2007

Ardin H Marschel 7/8/07
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER